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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/771,209	01/26/2001	Linda B. Buck	0575/38586-B/JPW/ADM/BJA	7352

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EXAMINER	
ULM, JOHN D	
ART UNIT	PAPER NUMBER
1646	10

DATE MAILED: 07/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/771,209	Applicant(s) Buck et al.
	Examiner John Ulm	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 6, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-24* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 7
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1) Claims 1 to 24 are pending in the instant application.

2) Claim 20 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. A properly dependant claim can not conceivably be infringed without infringing any of the claims from which it depends. Claim 20 can be infringed by a polypeptide composition which does not infringe the nucleic acid composition of any of the claims from which claim 20 depends. See M.P.E.P. 608.01(n)III.

3) The drawings in the instant application do not comply with 37 C.F.R. § 1.821(d), which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. M.P.E.P. 2422.02 expressly states that "when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings". Figure 5, for example, describes an amino acid sequence without employing a sequence identifier.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4) Claims 1 to 24 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure does not provide an adequate **written description** of a DNA encoding an odorant receptor lacking the entire amino acid sequence of any one of the twenty three amino acid sequences which are disclosed in the instant application. A comparison of those twenty three disclosed nucleotide and amino acid sequences as presented in Figures 9A to 31B of the instant application demonstrates that the sequence and structure of one DNA encoding an odorant receptor is not predictive of the sequence and structure of all odorant receptors. Whereas one would conclude that all odorant receptors belong to the G protein-coupled receptor family, the instant specification does not identify those properties which are common to all odorant receptor proteins which are not also found in G protein-coupled receptors which are not odorant receptors. The fact that DNAs encoding other odorant receptors can possibly be cloned by the disclosed method does not satisfy the written description requirement for a DNA which encodes such a receptor. Amgen Inc. v. Chugai Pharmaceuticals Co. Ltd., 18 U.S.P.Q. 2d, 1016, held that;

> "A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and describe how to obtain it. *See Oka,* 849 F.2d at 583, 7 USPQ2d at 1171. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, *e.g.,* encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that

> when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, *i.e.*, until after the gene has been isolated"

A claim which encompasses any isolated nucleic acid which encodes an odorant receptor, without reciting sufficient structural features so as to provide the required functions, constitutes nothing more than a wish to know the identity of any material with that biological activity. In the decision of *The Regents of the University of California v. Eli Lilly and Company,* 43 USPQ2d 1398 (CAFC 1997), the court held that:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood , 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel , 984 F.2d 1164, 1171, 25

USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Whereas the instant specification provides a detailed description of a small number of isolated DNAs encoding twenty three particular odorant receptors having very specific physical and structural properties, and the claims recite some of the structural features belonging to one or more of those twenty three specific receptors, the instant specification does not provide a structural formula which is definitive of all odorant receptors and certainly does not describe an isolate nucleic acid encoding an odorant receptor from a fish or dog, as required by the instant claims. The structural features recited in the claims are insufficient to define the genus of molecule recited because the majority of molecules which could be produced to meet the recited structural limitations would not be expected to function as odorant receptors. Whereas the instant specification may identify some properties which are common to some or all of the odorant receptors that are disclosed in the instant specification, it does not identify those defining structural elements which provide the functional and structural definition of the genus of molecules encompassed by the term "odorant receptor". See M.P.E.P. §§ 706.03(n) and 706.03(z).

5) Claims 1 to 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to **use** the invention

commensurate in scope with the claims. The only odorant receptor which is described in the instant specification in sufficient detail so as to permit an artisan to use it in a practical application is the odorant receptor identified therein as I7, which comprises the amino acid sequence presented in SEQ ID NO:76 of the instant application. The text in lines 15 to 25 on page 50 of the instant specification discloses a plurality of chemically related compounds which can be detected in a sample by employing a recombinant cell comprising a heterologous nucleic acid encoding I7. However, the instant specification does not provide the guidance needed to employ any other odorant receptor in a practical application.

The instant specification describes recombinant DNAs encoding a plurality of different proteins which are identified therein as odorant receptors (a.k.a. olfactory specific chemoreceptors). The identity of the proteins of the instant invention is based upon the fact that they are structurally related to those receptor proteins belonging to the G protein-coupled receptor family. Because of this structural similarity it is not unreasonable to conclude that the proteins of the instant invention are, in fact, G protein-coupled receptors. The identification of these proteins as odorant receptors is based exclusively upon the fact that they are specifically expressed in olfactory tissue. This is also not an unreasonable conclusion.

However, Applicant has not demonstrated the binding of a specific odorant to any one of the disclosed proteins, other than I7, and the induction of a signal as a result of that binding. More to the point, the instant specification provides a written description of a plurality of putative receptor proteins but, with the exception of I7, does not identify any ligand for any of those

receptors. In the absence of this information a practitioner can not used the claimed DNA in the manner disclosed since the ability to detect a ligand in a sample is meaningless if one does not know the identity or significance of the ligand being detected. Before a practitioner can use the instant invention they must first make a substantial inventive contribution by discovering a ligand for the receptor which is encoded by the claimed DNA. Because of the enormous number of possible chemical compounds which might serve as a ligand of that receptor, a practitioner would have to engage in a substantial amount of undue experimentation consisting of the screening an almost unlimited number of compounds in order to identify a receptor ligand. Since the instant application provides no guidance or working examples of a ligand for a receptor of the instant invention, beyond those compounds which bind I7, a practitioner does not have a reasonable expectation that such a ligand can be identified by simply screening large numbers of compounds. The instant specification is also devoid of guidance in predicting which compounds will serve in this capacity. Therefore, the instant specification does not provide the guidance needed to employ the vast majority of nucleic acids and proteins encompassed by the instant claims in a practical application. In other words, those nucleic acids that are encompassed by the instant claims and which do not encode I7 have no practical utility in currently available form.

6) Claims 1 to 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to **make** the invention commensurate in scope with the instant claims. The instant claims encompass isolated nucleic

acids encoding "odorant receptor proteins" having other than a native amino acid sequence, and the proteins encoded thereby. These claims encompass literally tens of thousands of embodiments of "odorant receptor protein", the vast majority of which do not occur in nature. However, the only functional odorant receptors which are described in the instant specification comprise one of those twenty three amino acid sequences described in the figures. Not a single working example of a nucleic acid encoding an "odorant receptor protein" which has been altered at even one amino acid residue is presented in the instant specification. Whereas the material limitations of the instant claims allow the amino acid sequence of the odorant receptor recited therein to deviate substantially from each of the twenty three naturally occurring proteins described therein, the instant specification does not provide the information needed to alter any one of those twenty three amino acid sequences at even one residue with a reasonable expectation that the resulting protein will retain functionality. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other

embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Before an artisan could predictably alter any one of the naturally occurring amino acids sequences described in the instant specification that artisan would have to know the identity of those amino acid residues in that naturally occurring sequence which are critical to the structural and functional integrity of an odorant receptor comprising that sequence and those residues which are expendable. Because the instant specification does not identify those amino acid residues in even one of the twenty three amino acid sequences described therein which are critical to the structural and functional integrity of an odorant receptor protein comprising that sequence, identify a structurally analogous protein for which this information is known and could be applied to an odorant receptor protein by extrapolation, or even provide a single working example of an intentionally modified protein of the instant invention, an artisan can not change even a single residue within any one of the twenty three naturally occurring the amino acid sequences presented in the instant specification and predict the effects of that change on the performance of that protein "by resort to known scientific law".

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

35 U.S.C. § 120 states that:

> An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application.

7) Claims 1 to 24 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by the Zhao et al. publication (SCIENCE 279:237-242, 09 Jan. 1998, cited by Applicant).

8) Claims 1 to 18 and 20 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by the Buck et al. publication (Cell 65:175-187, 1991). Buck et al. provided a written description of an isolated nucleic acid encoding I7, and the protein encoded thereby.

Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 120 from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the now claimed invention. Because application Serial Number 08/129,079 did not meet the requirements of 35 U.S.C. § 112, first paragraph, for those reasons of record in that application, it is unavailable under 35 U.S.C. § 120. As stated during the prosecution of application Serial Number 08/129,079 and essentially restated above:

> "The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to disclose how to use the claimed invention. The instant specification describes recombinant DNAs encoding a plurality of different proteins which are identified therein as odorant receptors (a.k.a. olfactory specific chemoreceptors). The identity of the proteins of the

instant invention is based upon the fact that they are structurally related to those receptor proteins belonging to the G protein-coupled receptor family. Because of this structural similarity it is not unreasonable to conclude that the proteins of the instant invention are, in fact, G protein-coupled receptors. The identification of these proteins as odorant receptors is based exclusively upon the fact that they are specifically expressed in olfactory tissue. This is also not an unreasonable conclusion.

However, Applicant has not demonstrated the binding of a specific odorant to any one of the disclosed proteins and the induction of a signal as a result of that binding. More to the point, the instant specification provides a written description of a putative receptor protein but does not identify any ligand for that receptor. In the absence of this information a practitioner can not used the claim DNA in the manner disclosed since the ability to detect a ligand in a sample is meaningless if one does not know the identity or significance of the ligand being detected. Before a practitioner can use the instant invention they must first make a substantial inventive contribution by discovering a ligand for the receptor which is encoded by the claimed DNA. Because of the enormous number of possible chemical compounds which might serve as a ligand of that receptor, a practitioner would have to engage in a substantial amount of undue experimentation consisting of the screening an almost unlimited number of compounds in order to identify a receptor ligand. Since the instant application provides no guidance or working examples of a ligand for a receptor of the instant invention a practitioner does not have a reasonable expectation that such a ligand can be identified by simply screening large numbers of compounds. The instant specification is also devoid of guidance in predicting which compounds will serve in this capacity."

Further, under current practice, the claims in application Serial Number 08/129,079 would be subject to a rejection under 35 U.S.C § 101 as being drawn to an invention without practical

utility in currently available form and, therefore, a mandatory rejection under the first paragraph of 35 U.S.C § 112, as indicated in M.P.E.P. 2107(II).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9) Claims 19 and 21 to 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Buck et al. publication (Cell 65:175-187, 1991). These claims differ from those above in requiring the isolated nucleic acid to be incorporated into an expression vector and host cell. Given the disclosure by Buck et al. that the amino acid sequence identified therein as I7 was that of an odorant receptor belonging to the protein-coupled receptor family, an artisan of ordinary would have found it *prima facie* obvious to have incorporated a recombinant nucleic acid encoding I7 into an expression vector and host cell to facilitate the possible identification of ligands thereto.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (703) 308-4008. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242 or (703) 872-9306. Official responses under 37 C.F.R. § 1.116 should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JOHN ULM
PRIMARY EXAMINER
GROUP 1800